## **ABSTRACT**

The present invention relates, in general, to attenuated negative-strand RNA viruses having an impaired ability to antagonize the cellular interferon (IFN) response, and the use of such attenuated viruses in vaccine and pharmaceutical formulations. The invention also relates to the development and use of IFN-deficient systems for selection of such attenuated viruses.

In particular, the invention relates to attenuated influenza viruses having modifications to the NS1 gene that diminish or eliminate the ability of the NS1 gene product to antagonize the cellular IFN response. The mutant viruses replicate in vivo but demonstrate reduced pathogenicity, and 15 therefore are well suited for live virus vaccines, and pharmaceutical formulations.

20

25

30

35